

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph beginning at page 11, line 25 has been amended as follows:

~~The invention will now be described in more detail with reference to the accompany drawings.~~

Paragraph beginning at page 4, line 21, has been amended as follows:

Figure 1 illustrates the plasmid pHD389; the ribosomal binding sequence, the sequence for the signal peptide from **ompA** and recognition sequence for several restriction enzymes are shown (SEQ ID NO: 14);

Paragraph beginning at page 4, line 24, has been amended as follows:

Figure 2 illustrates the amino acid (SEQ ID NO:3) and nucleic acid sequence (SEQ ID NO:4) for protein LG.

Paragraph beginning at page 5, line 6, has been amended as follows:

Figure 7 illustrates the amino acid (SEQ ID NO:6) and nucleic acid sequence (SEQ ID NO: 5) for protein M1.

Paragraph beginning at page 12, line 5, has been amended as follows:

It has been found that a protein L peptide (expressed in *E. coli*) constructed of the sequence ala-val-glu-asn (SEQ ID NO:15) domain B1 (from protein L) binds to the light chains of the immunoglobulins (W. Kastern, U. Sjöbring and L. Björck. 1992. Structure of peptostreptococcal protein L and identification of a repeated immunoglobulin light chain-binding domain. J. Biol. Chem. 267 (18):12820-5). Since this simple protein L-domain has a relatively

low affinity to Ig, ( $1 \times 10^7 \text{ M}^{-1}$ ), and since the naturally occurring protein L which is constructed of several mutually similar domains (B1-B5) has a high affinity to Ig ( $1 \times 10^{10} \text{ M}^{-1}$ ) four of these domains have been expressed together in the following way:

Paragraph beginning at page 12, line 13, has been amended as follows:

PL-N and PL-C1 are synthetic oligonucleotides (manufactured by the Biomolecular Unit at Lund University (Sweden) in accordance with applicant's instructions) which have been used to amplify a clonable gene fragment which is amplified with PCR (Polymerase Chain Reaction) and which codes for four Ig-binding protein L domains (ala-val-glu-asn-B1-B2-B3-B4-lys-lys-val-asp-glu-lys-pro-glu-glu, SEQ ID NO:1). Amino acids in the protein L-sequence are given for the primer which corresponds to the coded strand (PL-N):

PL-N: 5' -GCTCAGGCAGCGCCGGTAGAAAATAAGAAGAACACCAGAAC-3'

(SEQ ID NO:7)

valgluasnlysglugluthrproglu

(SEQ ID NO:8)

5'-end of this oligonucleotide is homologous with the coded strand in the protein L-gene (emphasized): those codons which code for the last three amino acids in the A-domain (val-glu-asn) are followed by the codons for the first six amino acids in the first of the Ig-binding domains in protein L (B1).

PL-C1: 5' -CAGCAGCA GGATTC TTATTATTCTTCTGGTTTTCGTCAACTTT

CTT-3' (SEQ ID NO:9)

Paragraph beginning at page 18, line 13, has been amended as follows:

PL-N and PL-C2 are synthetic oligonucleotides (manufactured at the Biomolecular Unit at Lund University (Sweden) in accordance with applicant's instructions)

which were used, with the aid of PCR (Polymerase Chain Reaction) to amplify a clonable gene fragment, called B1-4, which codes for four Ig-binding protein L domains (ala-val-glu-asn-B1-B2-B3-B4-lys-lys-val-asp-glu-lys-pro-glu-glu, SEQ ID NO:1):

PL-N: 5' -GCTCAGGC~~GGCGCCGGT~~AGAAAATAAGAAGAACACCAGAAAC-3'

(SEQ ID NO:7)

valgluasnlys~~g~~lugluthrproglu

(SEQ ID NO:8)

P1-C2: 5' -CAGCAGCAGCC~~ATGGTTCTCTGGTTTCGTCAACTTCTTA~~-3',

(SEQ ID NO:10)

Paragraph beginning at page 19, line 10, has been amended as follows:

It is known that a simple C-domain from protein G will bind to IgG (B. Guss, M. Eliasson, A. Olsson, M. Uhlen, A.-K. Frej, H. Jörnvall, I. Flock and M. Lindberg. 1986. Structure of the IgG-binding regions of streptococcal protein G. EMBO. J. 5: 1567-1575). The strength at which a simple C-domain binds to IgG is relatively low ( $5 \times 10^7 \text{ M}^{-1}$ ). A fragment which consists of two C-domains with an intermediate D-region having a length of 15 amino acids, however, has a considerably higher affinity to IgG ( $1 \times 10^9 \text{ M}^{-1}$ ). CDC-N and CDC-C are oligonucleotides which have been used as PCR-primers to amplify a clonable DNA-fragment, designated CDC, which codes for two IgG-binding protein G-domains (pro-met-asp-CDC-met).

CDC-N: GG ~~CCATGG~~ ACAC~~T~~ACAAATT~~A~~ATC~~CTT~~AATGGT

(SEQ ID NO:11)

metasp~~th~~rtyrl~~y~~lsleuileleua~~sngly~~

(SEQ ID NO:12)

CDC-C: C ~~AGGT~~CG ACTTATTAC~~ATTC~~CAGTTACCGTAAAGGTCTTAGT (SEQ ID  
NO:13)

In the Claims:

Claims 14 and 15 have been amended as follows:

14. (Thrice Amended) A protein having the ability to bind to the light chains of immunoglobulins, selected from the group consisting of:

(a) a protein comprising consisting essentially of the amino acid sequence of SEQ ID NO:1;

(b) a protein comprising consisting essentially of the amino acid sequence of at least one of the domains B1, B2, B3 or B4 of (a) wherein,

*why this change?* (i)(v) domain B1 is comprised of from amino acid 5 to amino acid 80 of SEQ ID NO:1;

(ii)(vi) domain B2 is comprised of from amino acid 81 to amino acid 152 of SEQ ID NO:1

(iii)(vii) domain B3 is comprised of from amino acid 153 to amino acid 224 of SEQ ID NO:1

(iv)(viii) domain B4 is comprised of from amino acid 225 to amino acid 296 of SEQ ID NO:1; and

(c) a protein comprising consisting essentially of the sequence of multiples or mixtures of the domains of B1, B2, B3 or B4 of (b).

15. (Amended) A hybrid protein comprising consisting essentially of one or more of the B1-B4 domains according to claim 14 which bind to the light chains in immunoglobulins of all classes, and domains which bind to heavy chains of immunoglobulin G.